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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-452]

Schedules of Controlled Substances: Temporary Placement of 4-Fluoroisobutyryl Fentanyl into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of intent.

SUMMARY: The Administrator of the Drug Enforcement Administration is issuing this notice of intent to issue a temporary order to schedule the synthetic opioid, *N*-(4-fluorophenyl)-*N*-(1-phenethylpiperidin-4-yl)isobutyramide (4-fluoroisobutyryl fentanyl or *para*-fluoroisobutyryl fentanyl), into Schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of this synthetic opioid into Schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. When it is issued, the temporary scheduling order will impose the administrative, civil, and criminal sanctions and regulatory controls applicable to Schedule I controlled substances under the Controlled Substances Act on the manufacture, distribution, reverse distribution, possession, importation, exportation, research, and conduct of instructional activities, and chemical analysis of this synthetic opioid.

DATES: The date of this notice of intent is [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

FOR FURTHER INFORMATION CONTACT: Michael J. Lewis, Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrisette Drive, Springfield, Virginia 22152; Telephone: (202) 598–6812.

SUPPLEMENTARY INFORMATION: This notice of intent is issued pursuant to the temporary scheduling provisions of 21 U.S.C. 811(h). DEA intends to issue a temporary order to add 4-fluoroisobutyl fentanyl to Schedule I under the Controlled Substances Act.¹ The temporary scheduling order will be published in the *Federal Register*, but that order will not be issued before [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER].

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. 21 U.S.C. 801–971. Titles II and III are referred to as the “Controlled Substances Act” and the “Controlled Substances Import and Export Act,” respectively, and are collectively referred to as the “Controlled Substances Act” or the “CSA” for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate

¹ Though DEA has used the term “final order” with respect to temporary scheduling orders in the past, this notice of intent adheres to the statutory language of 21 U.S.C. 811(h), which refers to a “temporary scheduling order.” No substantive change is intended.

medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, each controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause.

21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at 21 CFR part 1308.

Section 201 of the CSA, 21 U.S.C. 811, provides the Attorney General with the authority to temporarily place a substance into Schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if he finds that such action is necessary to avoid imminent hazard to the public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, 21 U.S.C. 812, or if there is no exemption or approval in effect for the substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. 21 U.S.C. 811(h)(1); 21 CFR part 1308. The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

Section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of his intention to temporarily place a substance into Schedule I of the CSA.² The Administrator transmitted notice of his intent to place 4-fluoroisobutyryl fentanyl in Schedule I on a temporary basis to the Assistant Secretary by letter dated January 5, 2017. The Assistant Secretary responded to this notice by letter dated January 17, 2017, and advised that based on a review by the Food and Drug Administration (FDA), there are currently no investigational new drug applications or approved new drug applications for 4-fluoroisobutyryl fentanyl. The Assistant Secretary also stated that the HHS has no objection to the temporary placement of 4-fluoroisobutyryl fentanyl into Schedule I of the CSA. 4-Fluoroisobutyryl fentanyl is not currently listed in any schedule under the CSA, and no exemptions or approvals are in effect for 4-fluoroisobutyryl fentanyl under section 505 of the FDCA, 21 U.S.C. 355. The DEA has found that the control of 4-fluoroisobutyryl fentanyl in Schedule I on a temporary basis is necessary to avoid an imminent hazard to the public safety.

To find that placing a substance temporarily into Schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Administrator is required to consider three of the eight factors set forth in 21 U.S.C. 811(c): the substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(h)(3). Consideration of these

² As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling may only be placed in Schedule I. 21 U.S.C. 811(h)(1). Substances in Schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. 21 U.S.C. 812(b)(1).

4-Fluoroisobutyryl Fentanyl

The chemical structure of 4-fluoroisobutyryl fentanyl was first described in 1999 in the scientific literature. No approved medical use has been identified for 4-fluoroisobutyryl fentanyl, nor has it been approved by the FDA for human consumption. The recent identification of 4-fluoroisobutyryl fentanyl in drug evidence and the identification of this substance in association with fatal overdose events indicate that this substance is being abused for its opioid properties.

Available data and information for 4-fluoroisobutyryl fentanyl, summarized below, indicate that this synthetic opioid has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. The DEA's three-factor analysis is available in its entirety under "Supporting and Related Material" of the public docket for this action at www.regulations.gov under Docket Number DEA-452.

Factor 4. History and Current Pattern of Abuse

The recreational abuse of fentanyl-like substances continues to be a significant concern. These substances are distributed to users, often with unpredictable outcomes.

4-Fluoroisobutyryl fentanyl has recently been encountered by law enforcement and public health officials and the adverse health effects and outcomes are demonstrated by fatal overdose cases. The documented negative effects of 4-fluoroisobutyryl fentanyl are consistent with those of other opioids. On October 1, 2014, the DEA implemented STARLiMS (a web-based, commercial laboratory information management system) to replace the System to Retrieve Information from Drug Evidence (STRIDE) as its laboratory drug evidence data system of record. DEA laboratory data submitted after September 30, 2014, are repositied in STARLiMS. Data from STRIDE and STARLiMS were queried on December 21, 2016. STARLiMS registered 21 reports containing 4-fluoroisobutyryl fentanyl, all reported in 2016, from Florida, Maryland, Mississippi, New Jersey, New York, Texas, and the District of Columbia. According to STARLiMS, the first laboratory submission of 4-fluoroisobutyryl fentanyl occurred in March 2016 in Maryland. The DEA is not aware of any laboratory identifications of 4-fluoroisobutyryl fentanyl prior to 2016.

The National Forensic Laboratory Information System (NFLIS) is a national drug forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by other federal, state and local forensic laboratories across the country. According to NFLIS, the only report of 4-fluoroisobutyryl fentanyl from state or local forensic laboratories was recorded in August 2016 in Pennsylvania. Due to normal lag time in reporting, NFLIS data from August through November 2016 is incomplete.³

³ Information was obtained from NFLIS on December 21, 2016.

Evidence suggests that the pattern of abuse of fentanyl analogues, including 4-fluoroisobutyryl fentanyl, parallels that of heroin and prescription opioid analgesics. Seizures of 4-fluoroisobutyryl fentanyl have been encountered in powder form and packaged similar to that of heroin. 4-Fluoroisobutyryl fentanyl has been encountered as a single substance as well as in combination with other substances of abuse, including heroin, fentanyl, furanyl fentanyl, methamphetamine, and cocaine. 4-Fluoroisobutyryl fentanyl has been connected to fatal overdoses, in which insufflation and intravenous routes of administration are documented.

Factor 5. Scope, Duration and Significance of Abuse

Reports collected by the DEA demonstrate 4-fluoroisobutyryl fentanyl is being abused for its opioid properties. This abuse of 4-fluoroisobutyryl fentanyl has resulted in morbidity and mortality (*see* DEA 3-Factor Analysis for full discussion). The DEA has received reports for at least 62 confirmed fatalities associated with 4-fluoroisobutyryl fentanyl. Information on these deaths, occurring as early as August 2016, was collected from post-mortem toxicology and medical examiner reports by the DEA. These deaths were reported from, and occurred in, Maryland. NFLIS and STARLiMS have a total of 22 drug reports in which 4-fluoroisobutyryl fentanyl was identified in drug exhibits submitted to forensic laboratories in 2016 from law enforcement encounters in Florida, Maryland, Mississippi, New Jersey, New York, Pennsylvania, Texas, and the District of Columbia. It is likely that the prevalence of 4-fluoroisobutyryl fentanyl in opioid analgesic-related emergency room admissions and deaths is underreported as standard immunoassays may not differentiate this substance from fentanyl.

The population likely to abuse 4-fluoroisobutyryl fentanyl overlaps with the population abusing prescription opioid analgesics and heroin. This is evidenced by the routes of drug administration and drug use history documented in 4-fluoroisobutyryl fentanyl fatal overdose cases. Because abusers of 4-fluoroisobutyryl fentanyl are likely to obtain this substance through unregulated sources, the identity, purity, and quantity are uncertain and inconsistent, thus posing significant adverse health risks to the end user. Individuals who initiate (i.e. use a drug for the first time) 4-fluoroisobutyryl fentanyl abuse are likely to be at risk of developing substance use disorder, overdose, and death similar to that of other opioid analgesics (e.g., fentanyl, morphine, etc.).

Factor 6. What, if Any, Risk There Is to the Public Health

4-Fluoroisobutyryl fentanyl exhibits pharmacological profiles similar to that of fentanyl and other μ -opioid receptor agonists. The toxic effects of 4-fluoroisobutyryl fentanyl in humans are demonstrated by overdose fatalities involving this substance. Abusers of 4-fluoroisobutyryl fentanyl may not know the origin, identity, or purity of this substance, thus posing significant adverse health risks when compared to abuse of pharmaceutical preparations of opioid analgesics, such as morphine and oxycodone.

Based on information received by the DEA, the abuse of 4-fluoroisobutyryl fentanyl leads to the same qualitative public health risks as heroin, fentanyl and other opioid analgesic substances. As with any non-medically approved opioid, the health and safety risks for users are great. The public health risks attendant to the abuse of heroin and opioid analgesics are well established and have resulted in large numbers of drug treatment admissions, emergency department visits, and fatal overdoses.

4-Fluoroisobutyryl fentanyl has been associated with numerous fatalities. At least 62 confirmed overdose deaths involving 4-fluoroisobutyryl fentanyl abuse have been reported from Maryland in 2016. As the data demonstrates, the potential for fatal and non-fatal overdoses exists for 4-fluoroisobutyryl fentanyl and 4-fluoroisobutyryl fentanyl poses an imminent hazard to the public safety.

Finding of Necessity of Schedule I Placement to Avoid Imminent Hazard to Public Safety

In accordance with 21 U.S.C. 811(h)(3), based on the available data and information, summarized above, the continued uncontrolled manufacture, distribution, reverse distribution, importation, exportation, conduct of research and chemical analysis, possession, and abuse of 4-fluoroisobutyryl fentanyl poses an imminent hazard to the public safety. The DEA is not aware of any currently accepted medical uses for 4-fluoroisobutyryl fentanyl in the United States. A substance meeting the statutory requirements for temporary scheduling, 21 U.S.C. 811(h)(1), may only be placed in Schedule I. Substances in Schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Available data and information for 4-fluoroisobutyryl fentanyl indicate that this substance has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. As required by section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), the Administrator, through a letter dated January 5, 2017, notified the Assistant Secretary of the DEA's intention to temporarily place this substance in Schedule I.

Conclusion

This notice of intent initiates a temporary scheduling process and provides the 30-day notice pursuant to section 201(h) of the CSA, 21 U.S.C. 811(h), of DEA's intent to issue a temporary scheduling order. In accordance with the provisions of section 201(h) of the CSA, 21 U.S.C. 811(h), the Administrator considered available data and information, herein set forth the grounds for his determination that it is necessary to temporarily schedule 4-fluoroisobutyryl fentanyl in Schedule I of the CSA, and finds that placement of this synthetic opioid substance into Schedule I of the CSA is necessary in order to avoid an imminent hazard to the public safety.

The temporary placement of 4-fluoroisobutyryl fentanyl into schedule I of the CSA will take effect upon publication of a temporary scheduling order, which will not be issued before [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER]. Because the Administrator hereby finds that it is necessary to temporarily place 4-fluoroisobutyryl fentanyl into Schedule I to avoid an imminent hazard to the public safety, the temporary order scheduling this substance will be effective on the date that order is published in the *Federal Register*, and will be in effect for a period of two years, with a possible extension of one additional year, pending completion of the regular (permanent) scheduling process. 21 U.S.C. 811(h)(1) and (2). It is the intention of the Administrator to issue a temporary scheduling order as soon as possible after the expiration of 30 days from the date of publication of this notice. Upon publication of the temporary order, 4-fluoroisobutyryl fentanyl will then be subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, importation, exportation, research, conduct of

instructional activities and chemical analysis, and possession of a Schedule I controlled substance.

The CSA sets forth specific criteria for scheduling a drug or other substance. Regular scheduling actions in accordance with 21 U.S.C. 811(a) are subject to formal rulemaking procedures done “on the record after opportunity for a hearing” conducted pursuant to the provisions of 5 U.S.C. 556 and 557. 21 U.S.C. 811. The regular scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions that conclude the regular scheduling process of formal rulemaking are subject to judicial review. 21 U.S.C. 877. Temporary scheduling orders are not subject to judicial review. 21 U.S.C. 811(h)(6).

Regulatory Matters

Section 201(h) of the CSA, 21 U.S.C. 811(h), provides for a temporary scheduling action where such action is necessary to avoid an imminent hazard to the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in Schedule I on a temporary basis. Such an order may not be issued before the expiration of 30 days from (1) the publication of a notice in the *Federal Register* of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of the proposed temporary scheduling order is transmitted to the Assistant Secretary of HHS. 21 U.S.C. 811(h)(1).

Inasmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be issued, the DEA believes that the notice and comment requirements of section 553 of the

Administrative Procedure Act (APA), 5 U.S.C. 553, do not apply to this notice of intent. In the alternative, even assuming that this notice of intent might be subject to section 553 of the APA, the Administrator finds that there is good cause to forgo the notice and comment requirements of section 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency to avoid an imminent hazard to the public safety.

Although the DEA believes this notice of intent to issue a temporary scheduling order is not subject to the notice and comment requirements of section 553 of the APA, the DEA notes that in accordance with 21 U.S.C. 811(h)(4), the Administrator will take into consideration any comments submitted by the Assistant Secretary with regard to the proposed temporary scheduling order.

Further, the DEA believes that this temporary scheduling action is not a “rule” as defined by 5 U.S.C. 601(2), and, accordingly, is not subject to the requirements of the Regulatory Flexibility Act (RFA). The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where, as here, the DEA is not required by section 553 of the APA or any other law to publish a general notice of proposed rulemaking.

Additionally, this action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordingly, this action has not been reviewed by the Office of Management and Budget.

This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with

Executive Order 13132 (Federalism) it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA proposes to amend 21 CFR part 1308 as follows:

PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES

1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), 956(b), unless otherwise noted.

2. In § 1308.11, add paragraph (h)(10) to read as follows:

§ 1308.11 Schedule I.

* * * * *

(h) * * *

(10) *N*-(4-fluorophenyl)-*N*-(1-phenethylpiperidin-4-yl)isobutyramide, its isomers, esters, ethers, salts and salts of isomers, esters and ethers (Other names: 4-fluoroisobutyl fentanyl, *para*-fluoroisobutyl fentanyl).....(9824)

Dated: March 16, 2017.

Chuck Rosenberg,
Acting Administrator.

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